PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (PCT/IPEA/416)
REP05544WO		
International application No.	International filing date *(day:month:year)*	Priority date *(day:month:year)*
PCT/GB97/03015	03/11/1997	01/11/1996
International Patent Classification (IPC) or national classification and IPC		
A61K38/44		
Applicant		
EUROGENE LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 12 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

I	☒	Basis of the report
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☒	Lack of unity of invention
V	☒	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability: citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☒	Certain defects in the international application
VIII	☒	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
14/04/1998	05.02.99
Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Brück, M Telephone No. (+49-89) 2399-8735

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB97/03015

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-64	as originally filed				

Claims, No.:

14-36	as originally filed				
1-13	as received on	19/10/1998	with letter of	16/10/1998	

Drawings, sheets:

1/3-3/3	as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☒ restricted the claims.
- ☒ paid additional fees.
- ☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:

see separate sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☒ all parts.

☐ the parts relating to claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	3,8,15,17-36
	No:	Claims	1-2,6-7,9-14,16
Inventive step (IS)	Yes:	Claims	17-35
	No:	Claims	1-16,36
Industrial applicability (IA)	Yes:	Claims	1-39,1-9*,14-15*,36* *cf. V.4/V.3 on SepSheet
	No:	Claims	

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

se separate she t

VIII. C rtain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Section IV:

1. The application as presently on file contains two separate inventions which are not so linked as to form a single general inventive concept (Rule 13.1 PCT):

   I. Claims 1-15

   Use of an agonist of a VEGF receptor or nucleic acid encoding it for the treatment or prevention of intimal hyperplasia of a blood vessel and implant.

   II. Claims 16-36

   A device for use in the delivery of a therapeutic agent to a blood vessel in a patient.

2. Independent claim 16 and dependent claims 17-35 claim a device for use in the delivery of any therapeutic agent. There is no connection or link to the agents such as nitric oxide synthase (or nucleic acid encoding it) or an agonist of a VEGF receptor (or nucleic acid encoding it) as claimed in invention I.
   Only claim 36 relates to a method for delivering an agent as defind in claims 1-15 using the delivery device according to claims 16-35
   Therefore, the device claimed in claims 16-35 is regarded as a separate invention.

INVENTION I:

Section V:

1. Reference is made to the following documents:

   D1 = Circulation, 1996, Vol. 94/8 suppl., abstract# 3720
   - the Publication Date of 15.10.1996 has been confirmed by the American Heart Asscіation, Phone: USA (214) 706 1347.

   D2 = WO 94/28721

D3 = Molecular Endocrinology, 1991, Vol. 5/12, pages 1806-1814

2. The present application does not meet the requirements of Article 33(2) PCT, because the subject matter of claim 1 and dependent claims 2, 6-7, 9, and 10-14 does not appear to be novel vis-à-vis document D1.

2.1 Claim 1 is directed to the second/ further medical use form, and relates to an agent that is an agonist of a receptor to which VEGF binds (cf. item VIII, 1.1 & 1.2) for the treatment/ prevention of intimal hyperplasia of a blood vessel, where the endothelium is wholly or largely intact.
Dependent claims 2-9 specify the blood vessel to be an artery (claim 2), the ailment to be stenosis induced by a surgical procedure or associated with pulmonary artery hypertension (claim 3); claim 4 specifies the surgical procedure to be angioplasty, coronary bypass surgery, surgical anastomosis or endarteriectomy; and claims 5 and 6 specify the ailment to be stenosis or restenosis. The agent is specified in claim 7 to be a protein having the function of human VEGF, or a nucleic acid encoding the protein; claim 8 specifies the sequence of the protein according to claim 7; and in claim 9 the agent is specified to be a nucleic acid in association with a viral or non-viral vector.

2.2 Document D1 discloses the treatment/ prevention of neointima formation in collared carotoid arteries ("a model that does not cause EC denudation" - line 5) by vascular endothelial growth factor (VEGF) (cf. items 1.1 & 1.2 in section VIII). The treatment of restenosis (lines 1 and 19) is achieved by gene transfer of the pCMV-VEGF plasmid into rabbit carotid arteries.
Therefore, claims 1-2, 6-7 and 9 do not appear to be novel vis-à-vis document D1.

2.3 Claim 14 (cf. item 1.3 in section VIII) is directed to the second/ further medical use form and relates to the agent as defined in any of the claims 6-9 for the treatment of a condition which can be treated or prevented by stimulation of NO or prostacyclin production *in vivo*.
However, this subject-matter has already been disclosed in document D1 as outlined in item 2.2.
Therefore, claim 14 does not appear to be novel vis-à-vis documents D1.

2.4 Claims 10-13 relate to an implant for therapeutic use, to be placed at or near the site of hyperplasia, and containing an agent as defined in any preceding claims (claim 10). The implant is described to be silastic implant or biodegradable (claim 11), in form of a collar for fitting around the blood vessel (claim 12), having an outer wall substantially impermeable to the agent comprised in it (claim 13).

However, it seems that such an implant has been disclosed in document D1 "... SMC proliferation was induced in rabbit carotid arteries by inserting an innert silicone collar around the arteries. VEGF-PI was applied directly in the silicone collar."

Therefore, claims 10-13 do not appear to be novel vis-à-vis document D1, either.

3. The present application does not meet the requirements of Article 33(3) PCT, because the subject matter of claim dependent claims 3-5, 8 and 15 does not appear to involve an inventive step vis-à-vis document D1, D2 and D3.

3.1 Dependent claims 3-5 relate to the diseases to be treated: stenosis induced by a surgical procedure or associated with pulmonary artery hypertension (claim 3); the surgical procedure is angioplasty (cf. item VIII, 1.4), coronary bypass surgery, surgical anastomosis or endarteriectomy (claim 4); or the condition is stenosis (claim 5).

The use of VEGF for the treatment of restenosis (where the endothelium is not denuded) as claimed in claim 1 is not novel (cf. item 2.2). The man skilled in the art knows that surgical procedures such as angioplasty leads to stenosis/ restenosis (see also document D2, page 2). Therefore, claims 3-5 do not appear to involve an inventive step.

3.2 Claim 8 specifies VEGF sequences for use in claim 7. However, the identical sequences are disclosed in document D3 in Figure 2B.
The use of VEGF in claim 7 is not novel (cf. item 2.3) and the specific VEGF sequences claimed are disclosed in document D3. Therefore, claim 8 does not appear to involve an inventive step.

3.3 Claim 15 specifies the condition in claim 14 to be hypertension.
The subject-matter of claim 14 is not novel (cf. item 2.4). Even though hypertension is not explicitly mentioned as disease condition in the prior art, document D2 describes on page 4 that "endothelium derived relaxing factor (EDRF)= NO is a potent vasodilatator, plays a key role in modulating conduit and resistance vessel tone, has important effects on cell growth and interactions of circulatory blood cells with a vessel wall, and that disturbances of EDRF activity may initiate or contribute to septic shock, hypertension, ..."
The skilled man faced with the technical problem--provision of a treatment for hypertension--would have combined the (known--cf. item 2.4) teaching from claim 14 (the agent as defined in any of the claims 6-9 is useful for the treatment of a condition which can be treated or prevented by stimulation of NO or prostacyclin production in vivo) with the above paragraph and thus treated hypertension with nitric oxide synthase or an VEGF receptor agonist.
Therefore, claim 15 does not appear to be inventive, either.

4. For the assessment of the present claims 1-9 and 14-15 as to the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims.
The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may, however, allow claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Section VIII:

1. The application does not fulfill the requirements of Article 6, because the following claims are unclear:

1.1. Claim **1** refers to the use of an agent which is only characterized by a function "an agent that is an agonist of a receptor to which VEGF binds" and renders. therefore, the claim unclear (Preliminary Examination Guidelines. C-III. 4.7a).

The agent should be clearly characterized.

1.2 The abbreviation "VEGF" used in claims **1 and 7** renders the claims unclear. It should be explained somewhere in the claims.

1.4 Claim **7** which is dependent on claim 1 is unclear due to the following: claim 1 refers to "intimal hyperplasia where the endothelium is wholly or largely intact." Claim 7 refers to angioplasty as the surgical procedure. However, it seems that the denudation of the blood vessel is unavoidable during a procedure of angioplasty as explained f.ex. in document D2 (page 2, lines 21-23).
This inconsistency should be overcome by the applicant.

1.3 Claim **14** refers to the use of an agent defined in claims 6-9 for the therapy of a condition that can be treated or prevented "... by stimulation of nitric oxide (NO) and/or prostacyclin production *in vivo.*" The condition to be treated is only characterized by a result to be achieved which renders the claim unclear (cf. PCT Preliminary Examination Guidelines, C-III, 4.7).
Therefore, the condition should be described in an unambiguous way.

INVENTION II:

Section V:

1. The documents referred to cf. INVENTION I, item V,1.

2. The present application does not meet the requirements of Article 33(2) PCT, because the subject matter of claim 16 does not appear to be novel vis-à-vis document D1.

2.1 Claim 16 relates to a device for delivering a therapeutic agent, comprising a body to provide a seal around the vessel and the agent associated with or held within so that it comes in contact with the adventitial surface of the vessel.

Document D1 describes a silicone collar put around the artery. The agent, the pCMV-VEGF plasmid, was directly applied into the collar on the adventitial side (abstract, lines 4, and 8-9).

Therefore, claim 16 does not appear to be novel vis-à-vis document D1.

2.2 Claim 36 relates to the method for delivering an agent as defined in INVENTION I in any of the claims 1-10 to a blood vessel with the device as described in any of the claims 16-35.

Document D1 describes the delivery of an agent as defined in claims 1-10 (cf. INVENTION I, V, 2.1) with a device as defined in any of claims 16 (cf. item V, 2.1). Therefore, claim 36 does not appear to be novel vis-à-vis document D1.

3. For the assessment of the present claim 36 as to the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims.
The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may, however, allow claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

4. However, dependent claims 17-35 appear to be novel and inventive. They specify the device in claim 16 as follows:
- defining a reservoir between the body wall and the vessel's adventitial surface filled with pharmaceutical formulation containing the agent (claim 17)
- the pharmaceutical formulation being a fluid or gel injectable to the reservoir (claim 18)
- the body portion is self-sealing (claim 19)
- the reservoir can contain up to 10 ml (claim 20)
- the thickness of the body part is constant, the reservoir being formed in use by ballooning of the first body portion (claim 21)

- the thickness is smaller in an intermediate portion which forms the reservoir (claim 22)
- the inner surface of the body comprises a sponge like material capable of being impregnated with the pharmaceutical formulation (claim 23)
- the inner surface of the body is impregnated with a pharmaceutical formulation containing the agent (claim 24)
- the body is biodegradable (claim 25)
- the material is gelatine, alginate, or collagen (claim 26)
- the body is moulded or extruded (claim 27)
- the body comprises flexible seal portions that can accommodate expansion of the bloodvessel caused by pulsatile blood flow (claim 28)
- the body comprises elongate seal portions 8-15 mm long (claim 29)
- the body is tubular (claim 30)
- the body is T- or Y shaped (claim 31)
- the body is X-shaped (claim 32)
- the body is arcuate (claim 33)
- the body has a longitudinal slit (claim 34)
- the body includes an inner layer or helical reinforcement (claim 35)

3.1 The claims are novel because no drug delivery device filled with a pharmaceutical formulation containing the agent has been described in the prior art.

3.2 For the evaluation of the involvement of an inventive step the following applies:

Document D1 describes an innert silicone collar around the arteries in which the agent (VEGF-PL) was directly applied. However, no details about the silicone collar are disclosed.

Document D4 discloses a drug delivery device with tapered ends, forming a sealed, closed reservoir. However, the drug is not filled into the reservoir by means of a gel like consistence or a sponge like material in the interior of the reservoir, but is introduced by inlet-outlet ports.

A skilled man faced with the technical problem--the provision of a local drug delivery system--could not have deduced from the prior art the solution of the

invention in the application which consists of a drug delivery device containing the agent in form of a gel introduced into the reservoir or through a sponge like material in the reservoir which is impregnated with the agent.

Therefore, claims 17-35 appear to involve an inventive step.

Section VII:

1. To meet the requirements of Rule 5.1(ii) PCT, the document D1 should be identified in the description and the relevant background art therein should be briefly discussed.

09/297486
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TRAITE DE COOPERATION EN MATIERE DE BREVETS

PCT

RAPPORT DE RECHERCHE INTERNATIONALE

(article 18 et règles 43 et 44 du PCT)

Référence du dossier du déposant ou du mandataire	**POUR SUITE A DONNER** voir la notification de transmission du rapport de recherche internationale (formulaire PCT/ISA/220) et, le cas échéant, le point 5 ci-après	
OA97131/SG		
Demande internationale n°	Date du dépôt international *(jour/mois/année)*	(Date de priorité (la plus ancienne) *(jour/mois/année)*
PCT/FR 98/ 01561	16/07/1998	01/09/1997
Déposant		
L'OREAL et al.		

Le présent rapport de recherche internationale, établi par l'administration chargée de la recherche internationale, est transmis au déposant conformément à l'article 18. Une copie en est transmise au Bureau international.

Ce rapport de recherche internationale comprend 3 feuilles.

[X] Il est aussi accompagné d'une copie de chaque document relatif à l'état de la technique qui y est cité.

1. [ ] **Il a été estimé que certaines revendications ne pouvaient pas faire l'objet d'une recherche** (voir le cadre I).

2. [ ] **Il y a absence d'unité de l'invention** (voir le cadre II).

3. [ ] La demande internationale contient la divulgation **d'un listage de séquence de nucléotides oud'acides aminés** et la recherche internationale a été effectuée sur la base du listage de séquence
   - [ ] déposé avec la demande internationale
   - [ ] fourni par le déposant séparément de la demande internationale
     - [ ] sans être accompagnée d'une déclaration selon laquelle il n'inclut pas d'éléments allant au-delà de la divulgation faite dans la demande internationale telle qu'elle a été déposée.
   - [ ] transcrit par l'administration

4. En ce qui concerne le titre,
   - [X] le texte est approuvé tel qu'il a été remise par le déposant.
   - [ ] Le texte a été établi par l'administration et a la teneur suivante:

5. En ce qui concerne l'**abrégé,**
   - [X] le texte est approuvé tel qu'il a été remis par le déposant
   - [ ] le texte (reproduit dans le cadre III) a été établi par l'administration conformément à la règle 38.2b). Le déposant peut présenter des observations à l'administration dans un délai d'un mois à compter de la date d'expédition du présent rapport de recherche internationale.

6. La figure **des dessins** à publier avec l'abrégé est la suivante:

   Figure n° _____
   - [ ] suggérée par le déposant.
   - [ ] parce que le déposant n'a pas suggéré de figure.
   - [ ] parce que cette figure caractérise mieux l'invention.

   [ ] Aucune des figures n'est à publier.

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

United States Patent and Trademark Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing: 14 May 1998 (14.05.98)	
International application No.: PCT/GB97/03015	Applicant's or agent's file reference: REP05544WO
International filing date: 03 November 1997 (03.11.97)	Priority date: 01 November 1996 (01.11.96)
Applicant: MARTIN, John, Francis et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International preliminary Examining Authority on:

14 April 1998 (14.04.98)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

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PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07K 14/00, A61K 38/00, 38/44, 38/19, 48/00 — A2

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Without international search report and to be republished upon receipt of that report.

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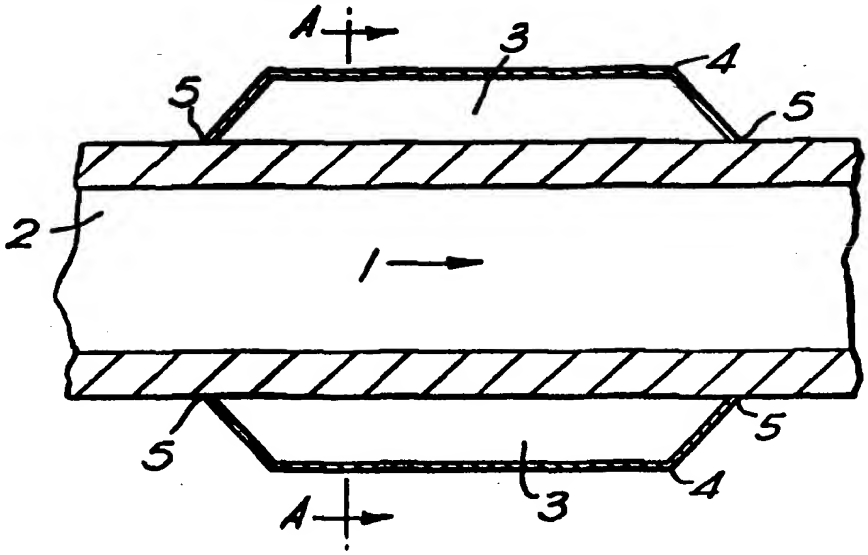
(54) Title: THERAPEUTIC USE OF GROWTH FACTOR, AND DELIVERY DEVICE, ESPECIALLY FOR THE TREATMENT OF INTIMAL HYPERPLASIA



(57) Abstract

Vascular endothelial growth factor (VEGF) has utility in the treatment of intimal hyperplasia, hypertension and atherosclerosis, and of conditions susceptible to treatment with agents that produce nitric oxide or prostacyclin. Instead of VEGF, an equivalent agent such as an agonist of VEGF receptors may be given, as may nucleic acid encoding such an agonist. The agent may successfully be administered *via* the adventitial surface of a blood vessel, e.g. using a device which defines a reservoir between the body wall and the vessel's adventitial surface, the reservoir being at least part-filled by a pharmaceutical formulation containing the agent to be delivered.

Replaced by Art 34

CLAIMS

1. Use of an agent that stimulates NO or prostacyclin production, for the manufacture of a medicament for the treatment or prevention of intimal hyperplasia of a blood vessel.

2. Use according to claim 1, wherein the blood vessel is an artery.

3. Use according to claim 1 or claim 2, for the treatment or prevention of stenosis induced by a surgical procedure or associated with pulmonary artery hypertension.

4. Use according to claim 3, wherein the surgical procedure is angioplasty, coronary bypass surgery, surgical anastomosis or endarteriectomy.

5. Use according to any preceding claim, for the treatment or prevention of stenosis or restenosis of the blood vessel.

6. Use according to any preceding claim, wherein the agent is a nitric oxide synthase, an agonist of a receptor to which VEGF binds, or a nucleic acid encoding the synthase or agonist.

7. Use according to any preceding claim, wherein the agent is a protein having the function of human VEGF, or a nucleic acid encoding the protein.

8. Use according to claim 7, wherein the protein has the sequence of SEQ. ID No. 2, 4, 6 or 8, or an active fragment thereof.

9. Use according to any of claims 6 to 8, wherein the agent is a nucleic acid in association with a viral or non-viral vector.

10. An implant for therapeutic use, adapted to be placed at or near the site of hyperplasia to be treated or prevented, and containing an agent as defined in any preceding claim.

11. An implant according to claim 10, which is a silastic implant or a biodegradable implant.

12. An implant according to claim 10 or 11, which is in the form of a collar for fitting around a blood vessel at or near the site of the hyperplasia to be treated or prevented.

13. An implant according to any of claims 10 to 12, having an outer wall substantially impermeable to the agent comprised in it.

RAPPORT DE RECHERCHE INTERNATIONALE

Demande Internationale No
PCT/FR 98/01561

A. CLASSEMENT DE L'OBJET DE LA DEMANDE
CIB 6 A61K7/13

Selon la classification internationale des brevets (CIB) ou à la fois selon la classification nationale et la CIB

B. DOMAINES SUR LESQUELS LA RECHERCHE A PORTE

Documentation minimale consultée (système de classification suivi des symboles de classement)
CIB 6 A61K

Documentation consultée autre que la documentation minimale dans la mesure où ces documents relèvent des domaines sur lesquels a porté la recherche

Base de données électronique consultée au cours de la recherche internationale (nom de la base de données, et si réalisable, termes de recherche utilisés)

C. DOCUMENTS CONSIDERES COMME PERTINENTS

Catégorie °	Identification des documents cités, avec, le cas échéant, l'indication des passages pertinents	no. des revendications visées
X	WO 96 15765 A (HENKEL KGAA ;ROSE DAVID (DE); HOEFFKES HORST (DE); MEINIGKE BERND) 30 mai 1996 cité dans la demande voir page 13; exemples B1-B3 ---	1
X	WO 96 15766 A (HENKEL KGAA ;ROSE DAVID (DE); HOEFFKES HORST (DE); MEINIGKE BERND) 30 mai 1996 cité dans la demande voir page 14; tableau 2 ---	1
X	DE 41 22 748 A (WELLA AG) 14 janvier 1993 voir le document en entier ---	1
X	EP 0 063 736 A (HENKEL KGAA) 3 novembre 1982 voir page 4, alinéa 3 ---	1

-/--

[X] Voir la suite du cadre C pour la fin de la liste des documents

[X] Les documents de familles de brevets sont indiqués en annexe

° Catégories spéciales de documents cités:

"A" document définissant l'état général de la technique, non considéré comme particulièrement pertinent

"E" document antérieur, mais publié à la date de dépôt international ou après cette date

"L" document pouvant jeter un doute sur une revendication de priorité ou cité pour déterminer la date de publication d'une autre citation ou pour une raison spéciale (telle qu'indiquée)

"O" document se référant à une divulgation orale, à un usage, à une exposition ou tous autres moyens

"P" document publié avant la date de dépôt international, mais postérieurement à la date de priorité revendiquée

"T" document ultérieur publié après la date de dépôt international ou la date de priorité et n'appartenenant pas à l'état de la technique pertinent, mais cité pour comprendre le principe ou la théorie constituant la base de l'invention

"X" document particulièrement pertinent; l'inven tion revendiquée ne peut être considérée comme nouvelle ou comme impliquant une activité inventive par rapport au document considéré isolément

"Y" document particulièrement pertinent; l'inven tion revendiquée ne peut être considérée comme impliquant une activité inventive lorsque le document est associé à un ou plusieurs autres documents de même nature, cette combinaison étant évidente pour une personne du métier

"&" document qui fait partie de la même famille de brevets

Date à laquelle la recherche internationale a été effectivement achevée	Date d'expédition du présent rapport de recherche internationale
21 décembre 1998	04/01/1999

Nom et adresse postale de l'administration chargée de la recherche internationale	Fonctionnaire autorisé
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